the immunofluorescence studies, and Dr V Biggs for her advice during the preparation of the manuscript.

[1] Anonymous. Acquired immunodeficiency syndrome [Editorial]. *Lancet* 1983;i:162-4.
[2] Levy JA, Ziegler JL. Acquired immunodeficiency syndrome is an opportunistic infection and Kaposi's sarcoma results from secondary immune stimulation. *Lancet* 1983;ii:78-81.
[3] Anonymous. Update on acquired immunodeficiency syndrome (AIDS)—United States. *MMWR* 1982;**31**:507-8.
[4] Brunet JB, Bouret E, Leiboustel J, *et al.* Acquired immunodeficiency syndrome in France. *Lancet* 1983;i:700.
[5] Mildvan D, Mathur U, Enlow RW, *et al.* Opportunistic infections and immune deficiency in homosexual men. *Ann Intern Med* 1982;**96**:700-4.

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Risk of giving intravenous aminophylline to acutely ill patients receiving maintenance treatment with theophylline

Drug monitoring has shown that the efficacy[1] of theophylline can be enhanced by maintaining the serum concentration at the upper end of the accepted therapeutic range (10-20 mg/l). Although the drug is safe when taken over long periods by patients in stable clinical states because its rate of clearance is constant, it may be toxic during acute illnesses, when its rate of clearance may suddenly fall.[2] Giving an intravenous bolus of aminophylline as emergency treatment to acutely ill patients increases the danger. This was illustrated by a recent case in which the serum theophylline concentration on admission was 64 mg/l before a bolus of aminophylline was given.[3] We undertook the present study to assess the risk of giving intravenous aminophylline to acutely ill patients already receiving oral theophylline.

Patients, methods, and results

Patients thought by the admitting officer to require emergency treatment with intravenous aminophylline were questioned about their regular drug treatment, and 25 who were receiving oral theophylline were studied. Eleven were subsequently treated with a continuous infusion of aminophylline. We recorded details of drug dosage, dosing interval, and the exact time the last tablet was taken. A 5 ml blood sample was taken, separated, and stored at −20°C for later analysis by enzyme immunoassay (EMIT).

We collected 26 samples from the 25 patients (one patient was admitted twice), who comprised 13 men and 12 women with exacerbations of bronchitis or asthma whose mean (SD) age was 61·7 (17) years. Three patients were smokers; no ex-smoker had smoked within the past three years. The mean daily dose of theophylline was 571 (202) mg (range 354-992 mg), and the mean time between the last dose and the blood sample was 7·7 (range 1-21) hours.

The table shows the serum theophylline concentrations, which ranged from 2 to 31·2 mg/l; they were below the therapeutic range in 10 samples and within the therapeutic range in 12. Four patients already had potentially toxic concentrations: two (cases 22 and 15, with concentrations of 25 mg/l and 31·2 mg/l) had been given 250 mg aminophylline intravenously by their general practitioners one and four hours respectively before admission. A third patient so treated (case 9) had a serum concentration of 11·9 mg/l four hours after the bolus injection, having taken his usual oral dose 10½ hours before giving the blood sample.

Comment

Although only four (16%) of these 25 patients presented with serum concentrations in the toxic range, a further nine (36%) had concentrations of over 11 mg/l; administration of 250 mg aminophylline in these patients, which raises the serum concentration by about 9 mg/l,[4] would have taken the concentrations into the toxic range. In 12 of the 26 samples the theophylline concentration was already within the therapeutic range, which raises the question of whether aminophylline treatment was appropriate. Considerable benefit may be obtained by maintaining the theophylline concentration close to 20 mg/l,[1] but some workers suggest that beta adrenergic agonists may be more effective in acute asthma.[5] For patients with initial concentrations of less than 10 mg/l an intravenous bolus followed by a maintenance infusion of aminophylline would clearly be beneficial, but monitoring of serum theophylline concentrations is necessary.

Details of daily doses of theophylline and serum concentrations after given times in 25 patients

Case No	Daily dose of theophylline (mg)	Time between dose and blood sample (hours)	Serum theophylline concentration (mg/l)
1	708	4½	11·8
2	354	21	11·2
3	708	9½	2·0
4	708	3	20·5
5	354	13½	10·8
6	354	7½	10·5
7	708	8	6·2
8	708	13	20·4
9	708	10½	11·9
10	354	12	3·5
11	708	9	14·1
12	354	2½	11·2
13	531	7½	2·0
14	708	2½	15·3
15	708	4†	31·2
16	992	10½	5·9
17	354	11	2·0
18	531	2	8·6
19	354	2	18·1
20	354	5	5·6
21	531	16	3·6
22	354	1‡	25·0
23	577	6	11·1
24	354	7½	9·2
25	885	2½	17·0
		4½	11·0

* 4 hours, † 1½ hours, ‡ 1 hour after aminophylline 250 mg given intravenously.

This study confirms that almost half the patients who regularly take theophylline are at risk from theophylline poisoning when given an intravenous bolus of aminophylline. When such patients are admitted to hospital acutely ill it would be safer to start a maintenance infusion equivalent to the oral dose and await the result of assay of serum theophylline concentrations before giving a bolus of the drug. Giving aminophylline to such patients may be hazardous when monitoring facilities are not available. Many patients do not require a bolus, and for others an aminophylline infusion is inappropriate.

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[1] Vozeh S, Kevitz G, Perruchoud A, *et al.* Theophylline serum concentration and therapeutic effect in severe acute bronchial obstruction: the optimal use of intravenously administered aminophylline. *Am Rev Respir Dis* 1982;**125**:181-4.
[2] Powell JR, Vozeh S, Hopewell P, Costello J, Scheiner LB, Reigelman S. Theophylline disposition in acutely ill hospitalised patients. *Am Rev Respir Dis* 1978;**118**:229-37.
[3] Thomson PJ, Hay JG. Dangers of compound drugs and intravenous aminophylline. *Lancet* 1982;ii:1228.
[4] Nicholson DP, Chick TW. A re-evaluation of parenteral aminophylline. *Am Rev Respir Dis* 1973;**108**:241-7.
[5] Rossing TH, Fanta CH, Goldstein DH, Snapper JR, McFadden ER. Emergency therapy of asthma: comparison of the acute effects of parenteral and inhaled sympathomimetics and infused aminophylline. *Am Rev Respir Dis* 1980;**122**:365-71.

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